

Role of Genotype in Cingulate Function and Inhibitory Control: a Functional Magnetic Resonance Imaging (fMRI) Study

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Monoamine-Oxidase-A (MAOA) is a neurotransmitter-metabolizing enzyme encoded by a gene which has previously been associated with aggression. When emphatically expressed, the word, “No,” is a salient signal to inhibit behavior. We hypothesized that in response to “No,” cingulate activity, which plays a key role in inhibitory control, will differ as a function of MAOA genotype. Twenty healthy subjects were genotyped to two groups: one with the genotype conferring low levels (L-MAOAs) and the other high levels (H-MAOAs) of MAOA activity. Subjects completed the Multidimensional-Personality-Questionnaire to obtain measures of self-reported aggression. During fMRI at 4-tesla, subjects were exposed to visual and emphatic auditory presentations of the word “No” and carefully selected control words. Both groups rated “No” as negatively valenced ($t=-3.8, p<.001$) compared to control words but L-MAOAs rated “No” as less intense than H-MAOAs ($t=2.55, p<.05$). L-MAOAs also showed reduced caudal cingulate in response to “No” ($t=3.9, p<.01$ cluster corrected) and the same cingulate area was correlated with subjects’ ratings of intensity to “No” ($r=.67, p<.01$). Although subjects did not differ on demographics, intelligence and depression, L-MAOAs had elevated aggression ($t=3.4, p<.01$) and these scores were associated with rostral cingulate activity specifically in response to “No” only in the L-MAOAs ($t=14.6, p<.005$ cluster corrected). Thus, subjects with low activity of the MAOA gene, reported elevated aggression and showed reduced behavioral and cingulate reactivity to “No,” as compared with subjects with high activity of this gene, suggesting that MAOA genotype has a role in aggressive behavioral phenotypes through modulation of the cingulate gyrus.